

## ADME NTP Study S0043 Dimethyl phthalate

The contractor used the abbreviation of DMP for the test article in the comparison tables.

Sex/Species: male F344 rats.

Vehicle: dermal, absolute ethanol.

CASRN 84-75-3

Radiolabeled with carbon-14 in the phthalyl moiety; Dimethyl phthalate, [<sup>14</sup>C-U-phthalyl]

Studies Performed:

- Single 33.75 mg/kg dermal dose to rats with covered dose site and sacrifice 7 days postdose. (n = 3)
- Single 33.75 mg/kg dermal dose to rats with uncovered dose site and sacrifice 7 days postdose. (n = 3)

The data of the 7-day excretion profile in the urine and feces for the dimethyl phthalate dosed rats with covered versus uncovered dose sites was given in a figure and is not shown here. The total recoveries for the dosed rats with covered or uncovered dose sites are shown in Table 2.

Dimethyl phthalate is one of nine phthalates that were tested together to determine excretion and tissue distribution after dermal administration. The comparison data is shown here with the dimethyl phthalate data (S0043). The other phthalates tested are:

- diethyl phthalate (DEP, CASRN 84-66-2)
- dibutyl phthalate (DBP, CASRN 84-74-2)
- diisobutyl phthalate (DIBP, CASRN 84-69-5)
- di-(n-hexyl) phthalate (DHP, CASRN 84-75-3)
- di(2-ethylhexyl) phthalate (DEHP, CASRN 117-81-7)
- diisodecyl phthalate (DIDP, CASRN 26761-40-0)
- butyl benzyl phthalate (BBP, CASRN 85-68-7)
- phthalic acid (PA, CASRN 88-99-3).

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Table 1. Excretion profile of Dimethyl phthalate in the urine and the feces after dermal application to the rat\*

Time (hr)	% Dose Excreted		
	Urine	Feces	Urine & Feces ( $\Sigma \bar{X}$ )
24	6.06 ± 0.52	0.125 ± 0.05	6.185
48	7.7 ± 5.5	0.97 ± 0.01	7.77
72	6.7 ± 1.9	0.17 ± 0.07	6.87
96	5.15 ± 0.6	0.129 ± 0.06	5.279
120	6.47 ± 2.5	0.207 ± 0.05	6.677
144	4.06 ± 1.2	0.1 ± 0.05	4.16
168	2.95 ± 2.7	0.08 ± 0.09	3.03
Total	39 ± 2.67	0.89 ± 0.23	39.89

\*Male F-344 rats (200 ± 20 gm) received dimethyl phthalate in ethanol dermally (33.75 mg/Kg). The skin was covered with a perforated plastic cap. Data points are the mean ± standard deviation. The percentage of dose excreted represents the fraction of the dose found (as <sup>14</sup>C-equivalent) relative to the total <sup>14</sup>C-equivalent applied.

Table 2. Tissue distribution of dimethylphthalate after  
7 days of dermal exposure

Tissue	% Dose Found ( $\bar{X} \pm S.D.$ )	
	Capped	Uncapped
Brain	0.016 $\pm$ 0.02	0.007 $\pm$ 0.005
Lung	0.009 $\pm$ 0.01	0.004 $\pm$ 0.002
Liver	0.047 $\pm$ 0.06	0.023 $\pm$ 0.029
Spleen	0.004 $\pm$ 0.04	0.002 $\pm$ 0.002
Small Intestine	0.014 $\pm$ 0.018	0.006 $\pm$ 0.007
Kidney	0.024 $\pm$ 0.03	0.004 $\pm$ 0.003
Testis	0.016 $\pm$ 0.018	0.006 $\pm$ 0.005
Fat	0.27 $\pm$ 0.27	0.106 $\pm$ 0.056
Muscle	0.6 $\pm$ 0.75	0.339 $\pm$ 0.386
Skin	0.4 $\pm$ 0.39	0.111 $\pm$ 0.069
Spinal Cord	0.003 $\pm$ 0.003	0.002 $\pm$ 0.002
Blood	0.156 $\pm$ 0.154	0.05 $\pm$ 0.048
Skin of Application	18.9 $\pm$ 22.7	0.128 $\pm$ 0.111
Plastic Cap	5.356 $\pm$ 2.87	---
Total Recovery	65.7 $\pm$ 26.235	21.748 $\pm$ 7.5

\*Total recovery represents the sum of the % dose found in the urine, the feces, the tissues and the plastic cap (if any) in 7 days.

\*Dose applied was 33.75 mg/kg.

Table 3. Total percentage recovery of the dose applied on the skin of the rat of the phthalate ester

Phthalate Ester	Phthalic Acid			Diethyl Phthalate			
	Low dose (capped) <sup>a</sup>	Medium dose (capped) <sup>a</sup>	Medium dose (uncapped) <sup>b</sup>	Low dose (capped) <sup>a</sup>	Low dose (uncapped) <sup>b</sup>	Medium dose (capped) <sup>a</sup>	High dose (capped) <sup>a</sup>
Total recovery*	81.08 ± 2.91	72.57	98.04	73.85 ± 21.377	26.194 ± 3.1	88.58 ± 19.1	77.57 ± 11.6

Phthalate ester	Dimethyl phthalate		Di-iso-butyl- <sup>a</sup> phthalate	Di-iso-butyl- <sup>a</sup> phthalate	Di-hexyl- <sup>a</sup> phthalate	Di-(2-ethyl- <sup>a</sup> hexyl)-phthalate	Di-iso-decyl <sup>a</sup> phthalate	Butyl Benzyl <sup>a</sup> phthalate
	Medium dose (capped) <sup>a</sup>	Medium dose (uncapped) <sup>b</sup>						
Total recovery	65.7 ± 26.23	21.76 ± 7.5	99.721 ± 3.092	92.94 ± 7.38	78.3 ± 6.06	105 ± 16.6	82.73 ± 12.15	86.85 ± 2.98

\*Total recovery represents the sum of the % dose found in the urine, the feces, the tissues, and the plastic cap (if any) in 7 days of exposure to the phthalate ester. Data represents the mean ± standard deviation, n = 3 except the medium dose level of phthalic acid where the data represents the mean, n = 2.

Table 4. Cumulative (urine) excretion profiles of the phthalate esters under investigation

Compound/Days	1	2	3	4	5	6	7
DMP	6.06	13.76	20.46	25.61	32.08	36.14	39.09
DEP	23.9	34.7	41.9	44.4	46.3	47.04	47.61
DBP	10.9	18.6	26.5	34.1	41	46.4	51.8
DIBP	6.3	15.4	23.3	30.1	34.9	39.77	42.23
DHP	1.38	4.43	7.5	10.12	12.46	14.94	16.24
DEHP	0.28	0.85	1.49	2.49	2.99		
DIDP	0.00	0.00	0.00	0.00	0.00	0.00	0.00
BBP	3.2	8.6	11.67	15.55	19.27	25.55	25.55
Phthalic acid	2.7	3.73	5.09	9.66	19.64	28.49	28.49

Data represents the % dose excreted (as  $^{14}\text{C}$ -equivalent) and they are the sum of the means of the % dose excreted in the urine.

Table 5. Cumulative feces excretion profiles of the phthalate esters under investigation

Compound/Days	1	2	3	4	5	6	7
DMP	0.125	0.195	0.365	0.496	0.701	0.801	0.88
DEP	1.03	1.825	2.11	2.21	2.3	2.36	2.4
DBP	1.13	2.83	4.63	5.93	6.99	7.93	8.9
DIBP	1	2.75	4.31	5.7	6.76	7.7	8.29
DHP	0.24	0.68	1.09	1.57	2.05	2.54	2.99
DEHP	0.14	0.34	0.63	1.32	2.12		
DIDP	0.04	0.097	0.157	0.219	0.317	0.39	0.49
BBP	0.41	1.12	1.7	2.335	2.97	3.67	4.27
Phthalic acid	0.12	0.44	0.95	1.69	7.29	17.09	22.89

Data represents the % of dose excreted (as  $^{14}\text{C}$ -equivalent) and they are the sum of the means of the % dose excreted in the feces.